AMENDMENTS TO THE CLAIMS

1. (Withdrawn - Currently Amended) A [[L]] liquid pharmaceutical formulation for the prolonged release of interleukin(s), this formulation comprising an aqueous colloidal suspension of low viscosity based on submicronic particles of water-soluble biodegradable polymer (PO) carrying hydrophobic groups (HG), said particles being non-covalently associated with ~~at least one interleukin and optionally with~~ at least one ~~other active principle~~ active principle (AP),

wherein at least one of the at least one active principle(s) is an interleukin, ~~characterized in that:~~

wherein the dispersion medium of ~~the~~ said aqueous colloidal suspension consists essentially of water,

wherein said formulation is capable of being injected parenterally and ~~then~~ forming a gelled deposit *in vivo*,

wherein the [[this]] formation of a gelled deposit[[:]] is ~~on the one hand being~~ at least partly caused by at least one physiological protein present *in vivo*, and ~~on the other hand making~~ makes it possible to prolong and control the *in vivo* release time of the AP beyond 24 h after administration,

wherein said formulation [[it]] is liquid under the injection conditions, and does not form a gelled deposit ~~it is also liquid~~ at the physiological temperature and/or physiological pH and/or in the presence of: a physiological electrolyte in a physiological concentration, and/or at least one surfactant .

2. (Withdrawn - Currently Amended) The [[F]] formulation according to claim 1, characterized in that its concentration of ~~[PO]~~ PO is set at a sufficiently high value to allow the formation of a gelled deposit *in vivo* after parenteral injection, in the presence of at least one physiological protein.

3. (Currently Amended) A [[L]] liquid pharmaceutical formulation for the prolonged release of ~~interleukin(s) and optionally other~~ at least one active principle(s) (AP),

wherein at least one of the at least one active principle(s) is an interleukin,

wherein ~~this~~ said formulation[[:]] ~~being~~ is liquid in the ambient atmosphere[[,]] ~~also being~~ and is liquid at [[the]] physiological temperatures, at ~~and/or~~ physiological pH, ~~and/or~~ in

the presence of [[:]] a physiological electrolyte in a physiological concentration, ~~and/or~~ or in the presence of at least one surfactant,

and wherein said formulation comprises [[comprising]] an aqueous colloidal suspension of low viscosity ~~based on~~ comprising submicronic particles of water-soluble biodegradable polymer PO carrying hydrophobic groups HG, wherein said submicronic particles ~~being~~ are non-covalently associated with at least one active principle AP, and wherein the dispersion medium of the aqueous colloidal suspension of low viscosity consists consisting essentially of water, and

wherein ~~characterized in that it's~~ the concentration of ~~[PO]~~ PO is ~~set at a~~ sufficiently high ~~value to allow the formation of a~~ such that a gelled deposit forms *in vitro* ~~after parenteral injection, in the presence of at least one protein~~ in an aqueous solution comprising bovine serum albumin in a concentration of 30 mg/ml.

4. (Currently Amended) The [[F]] formulation according to ~~any one of the preceding claims~~ claim 3, ~~characterized in that its~~ wherein the concentration of ~~[PO]~~ PO is ~~such that:~~ greater than or equal to 0.9 C1

~~• PO ≥ 0.9 C1,~~

~~• preferably 20.C1 ≥ [PO] ≥ C1,~~

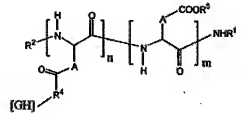
~~• and particularly preferably 10.C1 ≥ [PO] ≥ C1,~~

where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

5. (Currently Amended) The [[F]] formulation according to ~~any one of the preceding claims~~ claim 3, ~~characterized in that its~~ wherein the viscosity of the aqueous colloidal suspension is less than or equal to 5 Pa.s at 25°C.

6. (Currently Amended) The [[F]] formulation according to ~~any one of the preceding claims~~ claim 3, ~~characterized in that its~~ wherein the polymer PO is a polyamino acid ~~formed of~~ comprising aspartic units, ~~and/or~~ glutamic units, or both aspartic and glutamic units, wherein at least ~~some~~ one of ~~these~~ said unit [[s]] ~~carrying~~ carries at least one graft ~~grafts~~ ~~containing~~ comprising at least one hydrophobic group (HG).

7. (Currently Amended) The [[F]] formulation according to claim 6, wherein ~~characterized in that~~ the PO is ~~(are)~~ defined by general formula (I) below:



(I)

~~in which~~ wherein:

R^1 is selected from the group consisting of: H, a linear C2 to C10 alkyl, a [[or]] branched C3 to C10 alkyl, a benzyl, a terminal amino acid unit, and [[or]] -R^4-[HG];

R^2 is selected from the group consisting of: H, a linear C2 to C10 acyl, a [[or]] branched C3 to C10 acyl group, a pyroglutamate, and [[or]] -R^4-[HG];

R^3 is H or a cationic entity ~~preferably~~ selected from the group ~~comprising~~ consisting of: sodium metal cations ~~advantageously selected from the subgroup comprising sodium~~, potassium metal cations, calcium metal cations, ~~and~~ magnesium metal cations, ~~organic cations advantageously selected from the subgroup comprising:~~ organic cations based on amine, organic cations based on oligoamine, organic cations based on polyamine ~~(polyethylenimine being particularly preferred)~~, polyethylenimine, organic cations based on amino acid(s), ~~advantageously selected from the class comprising~~ organic cations based on lysine, [[or]] organic cations based on arginine, ~~and~~ cationic polyamino acids ~~advantageously selected from the subgroup~~ comprising polylysine and, cationic polyamino acids comprising oligolysine;

R^4 is a direct bond or a [[“]]spacer[[”]] based on 1 to 4 amino acid units;

A independently is a radical -CH_2- (aspartic unit) or -CH_2-CH_2- (glutamic unit);

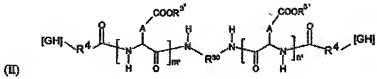
n/(n + m) is defined as the molar grafting rate and varies from 0.5 to 100 mol%;

~~wherein n/(n + m) is defined as the molar grafting rate and its value is sufficiently low for PO, dissolved in water at pH 7 and at 25°C, to form a colloidal suspension of submicronic particles of PO, n/(n + m) preferably being between 1 and 25 mol% and particularly preferably between 1 and 15 mol%;~~

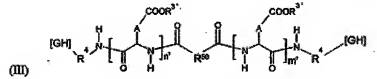
n + m varies from 10 to 1000 ~~and preferably between 50 and 300~~; and

HG is a hydrophobic group.

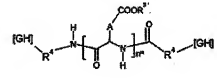
8. (Currently Amended) The [[F]] formulation according to claim 6, wherein ~~characterized in that~~ the PO has ~~(have)~~ one of general formulae (II), (III) and (IV) below:



(II)



(III)



(IV)

~~in which~~ wherein:

HG is a hydrophobic group;

R^{30} is a linear C2 to C6 alkyl group;

$R^{3'}$ is selected from the group consisting of: H, ~~or a cationic entity preferably selected from the group comprising:~~ sodium metal cations ~~advantageously selected from the subgroup comprising sodium~~, potassium metal cations, calcium metal cations, ~~and~~ magnesium metal cations, ~~organic cations advantageously selected from the subgroup comprising:~~ organic cations based on amine, organic cations based on oligoamine, organic cations based on polyamine ~~(polyethylenimine being particularly preferred)~~, organic cations based on amino acid(s), ~~advantageously selected from the class comprising~~ organic cations based on lysine, [[or]] organic cations based on arginine, ~~and~~ cationic polyamino acids ~~advantageously selected from the subgroup~~ comprising polylysine, and cationic polyamino acids comprising oligolysine;

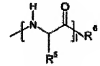
R^{50} is a C2 to C6 alkyl, dialkoxy, or diamine group;

R^4 is a direct bond or a [["]]spacer[["]] based on 1 to 4 amino acid units;

A independently is a radical $-CH_2-$ (aspartic unit) or $-CH_2-CH_2-$ (glutamic unit); and

n' + m' or n" is defined as the degree of polymerization and varies from 10 to 1000 ~~and preferably between 50 and 300~~.

9. (Currently Amended) The [[F]] formulation according to claim 7[[or 8]], ~~characterized in that the~~ wherein each [[n]] HG of the PO each independently of one another ~~are~~ is a monovalent radical ~~of~~ having the formula below:



(HG)

~~in which~~ wherein:

R^5 is selected from the group consisting of: a methyl group (alanine), an isopropyl group (valine), an isobutyl group (leucine), a sec-butyl group (isoleucine), and a [[or]] benzyl group (phenylalanine);

R^6 is a hydrophobic radical containing from 6 to 30 carbon atoms;

[[1]] l varies from 0 to 6.

10. (Currently Amended) The [[F]] formulation according to claim 9, ~~characterized in~~ wherein at least one ~~that all or some of the~~ hydrophobic ~~radicals~~ radical R^6 of the PO ~~are~~ is independently selected from the group of radicals consisting of ~~comprising~~:

a linear or branched alkoxy group containing from 6 to 30 carbon atoms;

a linear or branched alkoxy group containing (i) from 6 to 30 carbon atoms and (ii) ~~optionally containing~~ at least one heteroatom, ~~(preferably O and/or N and/or S) and/or~~ at least one unit of unsaturation, or both at least one heteroatom and at least one unit of unsaturation;

an alkoxy group containing 6 to 30 carbon atoms[[,]] and having one or more fused carbocyclic ring,

an alkoxy group containing 6 to 30 carbon atoms, having one or more fused carbocyclic rings, and ~~optionally~~ containing at least one unit of unsaturation, ~~and/or~~ at least one heteroatom, or both at least one heteroatom and at least one unit of unsaturation; ~~(preferably O and/or N and/or S),~~

an alkoxyaryl group or an aryloxyalkyl group having 7 to 30 carbon atoms; and

an alkoxyaryl group or an aryloxyalkyl group having 7 to 30 carbon atoms and ~~optionally~~ containing at least one unit of unsaturation, ~~and/or~~ at least one heteroatom, or both at least one heteroatom and at least one unit of unsaturation ~~(preferably O and/or N and/or S)~~.

11. (Currently Amended) The [[F]] formulation according to claim 9 or claim 10, wherein ~~characterized in that~~ the hydrophobic radical R^6 ~~of the graft of the PO~~ is derived from an alcohol precursor selected from the group consisting of ~~comprising~~ octanol, dodecanol, tetradecanol, hexadecanol, octadecanol, oleyl alcohol, tocopherol, and cholesterol.

12. (Currently Amended) The [[F]] formulation according to claim 6, ~~characterized in that~~ wherein the PO consists of an alpha-L-glutamate or alpha-L-glutamic homopolymer.

13. (Currently Amended) The [[F]] formulation according to claim 6, ~~characterized in that~~ wherein the PO consists of an alpha-L-aspartate or alpha-L-aspartic homopolymer.

14. (Currently Amended) The [[F]] formulation according to claim 6, ~~characterized in that~~ wherein the PO consists of an alpha-L-aspartate/alpha-L-glutamate or alpha-L-aspartic/alpha-L-glutamic copolymer.

15. (Currently Amended) The [[F]] formulation according to claim 14, ~~characterized in that, in the PO, the~~ wherein the PO comprises a distribution of ~~the aspartic and/or glutamic units carrying grafts containing at least one HG unit~~ aspartic units carrying at least one HG unit, glutamic units carrying at least one HG unit, or both aspartic units carrying at least one HG unit and glutamic units carrying at least one HG unit is such that the resulting polymer is ~~either~~ random, [[or]] of the block type, or of the multiblock type.

16. (Withdrawn - Currently Amended) The [[F]] formulation according to claim 1, characterized in that the molecular weight of the PO is between 2000 and 100,000 g/mol ~~and preferably between 5000 and 40,000 g/mol~~.

17. (Currently amended) The [[F]] formulation according to claim 7, ~~characterized in that~~ wherein the hydrophobic radical R^6 ~~of the graft of the PO~~ is derived from ~~an alcohol precursor formed of~~ tocopherol, and ~~in that~~ wherein[[:]]

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$, and

~~preferably $3.5\% \leq [n/(n+m)] \times 100 \leq 7.5\%$,~~

n + m varies from 100 to 400 ~~and preferably between 120 and 300~~.

18. (Currently Amended) The [[F]] formulation according to claim 7, ~~characterized in that~~ wherein the hydrophobic radical R^6 ~~of the graft of the PO~~ is derived from ~~an alcohol precursor formed of~~ cholesterol:

$1\% \leq [n/(n+m)] \times 100 \leq 10\%$, and

~~preferably $3.5\% \leq [n/(n+m)] \times 100 \leq 6.5\%$,~~

n + m varies from 100 to 400 ~~and preferably between 120 and 300~~.

19. (Currently Amended) The [[F]] formulation according to claim 7 ~~17 or 18~~, ~~characterized in that~~ wherein the concentration of polymer ~~[PO]~~ PO is between 15 and 50 mg/ml.

20. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 19~~ claim 3, ~~characterized in that~~ wherein the viscosity of the aqueous colloidal suspension is less than or equal to 5 Pa.s at 25°C.

21. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 20~~ claim 3, ~~characterized in that~~ wherein the ~~hydrophobically modified polymers~~ polymer PO [[are]] is selected from the group consisting of: ~~comprising~~ polyamino acids, polysaccharides, ~~(preferably those in the subgroup comprising~~ pullulans, ~~and/or~~ chitosans, ~~and/or~~ mucopolysaccharides[[)]], gelatins, and mixtures thereof.

22. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 21~~ claim 3, ~~characterized in that~~ wherein [[it's]] the % weight fraction of interleukin(s) not associated with the submicronic particles ~~[non-associated interleukin(s)], in %,~~ is ~~such that: [non-associated interleukin(s)]~~ $\leq$ 1, ~~preferably [non-associated interleukin(s)] $\leq$ 0.5, most preferably [non-associated interleukin(s)] $\leq$ 0.1~~.

23. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 22~~ claim 3, ~~characterized in that~~ wherein the interleukin is interleukin 2.

24. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 23~~ claim 3, ~~characterized in that~~ further comprising ~~the additional~~ at least one active principle(s) ~~other than the interleukin(s) is (are)~~ selected from the group consisting of a protein, a glycoprotein, a protein bonded to one or more polyalkylene glycol chains, ~~[preferably~~ polyethylene glycol

(PEG) chains, ~~: "PEGylated protein"]~~, a polysaccharide, a liposaccharide, an oligonucleotide, a polynucleotide, [[or]] a peptide, ~~this (these) additional active principle(s) preferably being selected from~~ haemoglobins, cytochromes, albumins, interferons, cytokines, antigens, antibodies, erythropoietin, insulin, growth hormones, factors VIII and IX, haemopoiesis stimulating factors, and mixtures thereof.

25. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 24~~ claim 3, ~~characterized in that~~ wherein said formulation [[it]] is injectable by the parenteral route, by the subcutaneous route, by the intramuscular route, by the intradermal route, by the intraperitoneal route, [[or]] by the intracerebral route, or into a tumour.

26. (Currently Amended) The [[F]] formulation according to ~~any one of claims 1 to 25~~ claim 3, ~~characterized in that~~ wherein said formulation [[it]] is intended for the preparation of drugs~~, particularly for administration~~ administered by the parenteral route, by the subcutaneous route, by the intramuscular route, by the intradermal route, by the intraperitoneal route, [[or]] by the intracerebral route ~~or into a tumour, or~~ by the oral route, by the nasal route, by the vaginal route, [[or]] by the ocular route, or into a tumour,.

27. (Withdrawn - Currently Amended) A [[P]] process for the preparation of drugs, particularly for administration by the parenteral, subcutaneous, intramuscular, intradermal, intraperitoneal or intracerebral route or into a tumour, or by the oral, nasal, vaginal or ocular route, characterized in that it consists essentially in using at least one formulation according to ~~any one of claims~~ claim 3 ~~1 to 26~~.

28. (Withdrawn - Currently Amended) A [[D]] derived product, ~~characterized in that it comprises~~ comprising submicronic particles formed of non-covalent PO/AP associations as defined in claim 1~~, and in that it is obtained from the formulation according to any one of claim[[s]] 1 to 26~~.

29. (Withdrawn - Currently Amended) The [[D]] derived product according to claim 28, ~~characterized in that~~ wherein said formulation [[it]] ~~consists of~~ comprises a powder or a gel.

30. (Withdrawn - Currently Amended) ~~Process~~ A method for the preparation of the formulation according to ~~any one of claims 1 to 26~~ claim 3, said method ~~characterized in that it consists essentially in~~ comprising the steps of:

~~taking~~ preparing a colloidal suspension of nanoparticles comprising [[of]] at least one PO,

mixing ~~this~~ said colloidal suspension of nanoparticles ~~of~~ comprising at least one PO with at least one interleukin ~~(and one or more other possible active principles)~~ and at least one additional active principle(s) (AP), ~~preferably~~ in aqueous solution,

~~optionally~~ adding at least one excipient,

adjusting the pH, ~~and/or~~ the osmolarity , or both ~~if necessary~~, and

~~optionally~~ filtering the resulting suspension.

31. (Withdrawn - Currently Amended) ~~Process~~ The method according to claim 30, characterized in that the at least one additional AP is ~~(are)~~ in the form of an aqueous suspension or solution ~~for mixing with the colloidal suspension of nanoparticles of PO~~.

32. (Withdrawn - Currently Amended) ~~Process~~ A method for the preparation of the formulation according to ~~any one of claims1 to 26~~ claim 3, ~~characterized in that it~~ said method comprising the steps of ~~consists essentially in~~:

~~taking~~ making a powder comprising [[of]] at least one polymer PO,

mixing ~~this~~ said powder with an aqueous suspension or solution [[of]] comprising at least one interleukin and at least one ~~(and one or more other possible active principles), preferably~~ additional active principle(s) in aqueous solution,

~~optionally~~ adding at least one excipient,

adjusting the pH, ~~and/or~~ the osmolarity, or both ~~if necessary~~, and

~~optionally~~ filtering the resulting suspension.

33. (Withdrawn - Currently Amended) ~~Process~~ A method for the preparation of [[the]] a pharmaceutical formulation ~~according to any one of claims 1 to 26 characterized in that it~~ said method comprising the steps of ~~consists essentially in~~:

~~taking a powder produced by~~ drying the liquid formulation according to ~~any one of any one of claims 1 to 26~~ claim 3 to produce a powder,

mixing ~~this~~ said powder with an aqueous liquid medium, ~~preferably with stirring,~~

~~optionally~~ adding at least one excipient,

adjusting the pH, ~~and/or~~ the osmolarity, or both ~~if necessary~~, and

~~optionally~~ filtering the resulting suspension.

34. (Withdrawn - Currently Amended) ~~Process~~ A method for the preparation of a powder pharmaceutical formulation ~~derived from the formulation according to any one of claims 1 to 26, characterized in that said powder is obtained by~~ said method comprising the step of drying the formulation according to ~~any one of claims 1 to 26~~ claim 3.

35. (New) The formulation according to claim 3, wherein the concentration of PO is greater than or equal to C1 and is less than or equal to 20.C1, where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

36. (New) The formulation according to claim 3, wherein the concentration of PO is greater than or equal to C1 and is less than or equal to 10.C1, where C1 is the "induced gelling" concentration of the particles of PO, as measured in an IG test.

37. (New) The formulation according to claim 7, wherein the molar grafting rate is sufficiently low for PO, dissolved in water at pH 7 and at 25°C, to form a colloidal suspension of submicronic particles of PO.

38. (New) The formulation according to claim 7, wherein $n/(n + m)$ is being between 1 and 25 mol%.

39. (New) The formulation according to claim 7, wherein $n/(n + m)$ is being between 1 and 15 mol%.

40. (New) The formulation according to claim 7, wherein $n + m$ is between 50 and 300.